

Valid methods: the quality assurance of test method development, validation, approval, and transfer for veterinary testing laboratories

Ann L. Wiegers

Abstract. Third-party accreditation is a valuable tool to demonstrate a laboratory's competence to conduct testing. Accreditation, internationally and in the United States, has been discussed previously. However, accreditation is only 1 part of establishing data credibility. A validated test method is the first component of a valid measurement system. Validation is defined as confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled. The international and national standard ISO/IEC 17025 recognizes the importance of validated methods and requires that laboratory-developed methods or methods adopted by the laboratory be appropriate for the intended use. Validated methods are therefore required and their use agreed to by the client (i.e., end users of the test results such as veterinarians, animal health programs, and owners). ISO/IEC 17025 also requires that the introduction of methods developed by the laboratory for its own use be a planned activity conducted by qualified personnel with adequate resources. This article discusses considerations and recommendations for the conduct of veterinary diagnostic test method development, validation, evaluation, approval, and transfer to the user laboratory in the ISO/IEC 17025 environment. These recommendations are based on those of nationally and internationally accepted standards and guidelines, as well as those of reputable and experienced technical bodies. They are also based on the author's experience in the evaluation of method development and transfer projects, validation data, and the implementation of quality management systems in the area of method development.

Laboratory data credibility has 3 components. These are a validated method, proficiency testing, and third-party accreditation. Proficiency testing is used to verify that the analyst can conduct the method and to compare results with those of other laboratories. Third-party accreditation is used to verify that the laboratory is competent to conduct the testing and that the method validation has been done within the environment and requirements of a quality management system. These components help ensure that the methods used by the laboratory are valid. For a method to be viewed as valid, the following should be ensured:

- The method is properly selected.
- A project management system is in effect during development and validation.
- The method is optimized.
- Critical control points of the method are known, and therefore the process control and quality control necessary for the method are also known.
- The method is in statistical control.
- The method uses or is traceable to national and international reference materials and measurement standards.
- Measurement uncertainties are known for the testing process and for the method validation.
- The performance characteristics of the method are known and are well supported with data.
- A collaborative trial is done.
- The method and test process are fully documented in a procedure that contains adequate information and is clear.
- The client(s) of the laboratory have opportunities for input and have given informed consent concerning the method selection, development, and validation at critical and appropriate times.
- Records are secure and can recreate events.
- Approvals during development and approvals for use have been done by qualified staff.
- The method is developed, validated, approved, and transferred according to approved general procedures and criteria for such activities.
- Proficiency criteria are in place and proficiency testing is available.
- The work has been done in the environment of a quality management system.

Method development, validation, approval, and transfer conducted in a quality management environment not only ensure that methods and test results are viewed as valid but also contribute to the well-being of the laboratory by ensuring that the work is done efficiently, effectively, consistently, dependably, and

From the National Veterinary Services Laboratories and Center for Veterinary Biologics, USDA, APHIS, VS, 1800 Dayton Avenue, Ames, IA 50010.

that the choice of method is defensible. In addition, waste may be minimized, client satisfaction ensured, deadlines met, and the laboratory placed in a better position to defend the validity of its data and opinions. The creation of a quality management system that covers method development and validation is a necessary investment by the laboratory. Knowledge costs money and so do loss of proprietary rights and litigation. Loss of time wastes careers. Loss of credibility is difficult to recover. Quality control does not do much for quality if the test is not valid, and it is not helpful to the client to have developed or to use the wrong method.

Method development

Selection of the test method. To ensure that a method is properly selected for use, the following activities are recommended.

- 1) A review and setting of priorities by the laboratory or its organization.
- 2) Accurate identification of the client's needs. ISO/IEC 17025¹⁶ states "shall include a clear specification of the client's requirements." Factors such as use, cost, desired performance characteristics, and turnaround time should be included in discussions with the client. Of these, the proposed use of the method is probably the most important consideration. Uses include the following:
 - Single-animal or herd test.
 - Screening or confirmatory test.
 - Management of an outbreak or surveillance of a population declared free of a particular disease.
 - Use in the field, in a factory or slaughterhouse, by a contract laboratory, or by a research laboratory.
 - For checking of product lots.
 - For export certification.
 - For a live or a dead animal.
 - For a pooled sample or for single samples.
 - For routine or nonroutine testing.
 - For a small or large number of samples.
 - For a particular type of sample (species, tissue, matrix, with interfering substances, etc.).
- 3) Establishment of criteria and implementation of procedures for submission of proposals for development, to ensure adequate information for decisions. Examples of contents of proposals include the following:
 - Logistical information (e.g., proponent's name, address, institution, the reason for development of the method).
 - The identification of the client(s).
 - The identification of key roles such as those of the study director or principal investigator.
 - A description of the project.

- A detailed description of the experimental design.
 - Characteristics to be determined and the methods to be used for the determination.
 - Statistics to be used.
 - Records to be kept (e.g., logbooks, worksheets, procedures).
 - Materials needed (e.g., test materials, reagents, reference materials).
 - A full description of the study material(s) (e.g., porcine muscle).
 - The equipment needed.
 - Safety considerations and needs.
 - Environmental needs (e.g., biosecurity level, humidity, temperature range, special disposal systems).
 - Technical support needed.
 - Time frames.
 - Time lines.
 - Costs.
- 4) Review of proposals by an informed, qualified group that represents the interests of the laboratory and possibly also of the client.
 - 5) Criteria and procedures for the selection of proposals for development.

A project management system. If a laboratory is to include method development and validation in its quality management system, it is essential to have a project management system. A project management system is advisable for research and development to run smoothly.^{7,20} ISO International Standard 10006¹⁵ describes the requirements for achieving quality in project management. Components of a project management system include the following:

- A project numbering system (a unique number that has been assigned to the project should be on all documents and data records relating to a development and validation project).
- Policies and procedures for management of projects.
- A communications control system.
- Policies and procedures that define and describe the authority for decisions on progress, approval of data, and approval of designs.

The laboratory should also have policies and general procedures on how research, development, and validation will be conducted (e.g., requirements for laboratory notebooks and technical procedures, assigned and documented roles and responsibilities, the sequence of steps that must take place during development, and what is necessary for approval at each critical step). These should include the requirement for auditing of records by the quality department during the project to ensure that company policies and pro-

cedures are being followed during the conduct of the project, especially with regard to records keeping. These policies and procedures should be approved by those responsible for the research management program at the highest level of management of the laboratory. The assignment of specific titles relevant to activities, roles and responsibilities, and authorities is recommended (e.g., “Principal Investigator,” “Study Director,” and “Quality Assurance Manager”). For each project, the research scientist or developer should write or make specific reference to all general and technically specific procedures necessary to conduct the scientific work (e.g., procedures for making phosphate buffered saline and operating equipment). The Organisation for Economic Cooperation and Development (OECD) Principles of Good Laboratory Practice (GLPs)¹⁹ and the AOAC International (formerly the Association of Official Analytical Chemists) Official Methods of Analysis (OMA) Program¹ are considered good models although they are not equivalent.

Records. As previously stated, the developer should make and keep up-to-date a list of all records to be kept. Examples of records to be kept and identified by the project number include the following:

- Laboratory notebooks.
- Databases.
- Forms.
- Work notes.
- Checklists and checksheets.
- Worksheets and other process control and quality control records.
- Original observations.
- Derived data.
- Control charts and graphs.
- Interpretations and opinions.
- Procedures used to do the work.
- Relevant communications.
- Sample/test material records.
- Sampling records/sourcing records.
- Equipment records.
- Reagents records.
- Environmental records.
- Animal records.
- Literature cited.
- Copies of references.
- A description of the logical decision-making criteria/discussion of the logic behind decisions (typically in the laboratory notebook).
- Approvals and other official letters and memoranda.
- Records of meetings, actions, and decisions.
- Audit records.
- Calculations.
- External and internal test reports.

- Calibration certificates.
- Clients’ notes, papers, and feedback.
- Contracts.

Records keeping. A detailed discussion of records keeping requirements, systems, and management is beyond the scope of this article. However, a few topics warrant a brief discussion.

The laboratory will need policies and procedures on records and data-keeping practices, archiving systems and practices, legal and patent concerns, confidential business information, and other security issues.

Worksheets and other pertinent records should be dated and signed. Care should be taken to ensure that such records contain all relevant data to completely reproduce events. For example, a record of the weight of a chemical used should include the balance identification number. This enables an investigator to confirm that the balance was in calibration. Cross-references to quality documents should include the identification and version number of the document.

All original observations should be recorded or saved. Examples of original observations include those of optical density or titer (e.g., a color change), photographs, gels, whether an animal was dead or alive, and the presence of an agent, stain, or phenomenon (e.g., a gross pathological or histopathological observation).

All records must be indelible (no pencil), durable, legible, clear, complete, continuous (have continuity), unambiguous, traceable, secure, and retrievable, and have integrity (the last is particularly important for electronic records). Backups should exist, preferably at another site. Records should be verified (signed) and if applicable, witnessed. Changes must be done so that the previous entry is readable and relatable to the entry that alters or replaces it. For paper records, this is done by marking a single line through the old entry or observation, writing the new observation near it, and dating and initialing near the change. In some cases, it is advisable to include the reason for the change. Unused pages and blank areas of worksheets should be marked through with a diagonal line.

Once a test method development project is completed, all records should be assembled, checked for completeness, legibility, traceability, and continuity and then archived according to laboratory procedure. Archiving is an important quality assurance activity. A full discussion of archiving facilities and practices and of the care and handling of various types of records is beyond the scope of this article but it should be reiterated that records must be readily retrievable, complete, and usable.

The laboratory notebook. The laboratory notebook is an essential record and project management tool. A

full discussion of the criteria for and use of laboratory notebooks and laboratory notebook systems is beyond the scope of this article. There is an excellent book on the subject.¹⁷

Traditionally, the laboratory notebook held data and observations. It still can, but nowadays, for projects, it functions more as a valuable tool to pull the project together in a logical and continuous time line, as well as a reference to where data and observations may be found (e.g., databases and procedure numbers). The laboratory notebook may be used to track project progress and document thoughts, ideas, plans, designs, logic, conclusions, and decisions through the project time line. It should be started when the researcher is thinking about the project, before the proposal (e.g., when the literature search starts), not with the commencement of data gathering. In short, contents should be verifiable, say what was done and when, make it clear who did the work, and enable someone else to do the same thing at some future date.⁹

Laboratory notebooks should be hardbound, durable, and the pages sequentially numbered. The binding should be of such a quality to ensure no loss of pages during use and storage. The paper must be of such a quality to ensure that it lasts the required time. In short, a laboratory notebook should be durable.

Laboratory notebooks should be controlled. That is, because it is essential to the laboratory that all notebooks can be accounted for and readily located and retrieved, they should be issued from a central office and be uniquely and continuously numbered. The laboratory should have policies and procedures for notebook specifications, issuance, and use. It is recommended that each notebook have a single user for method development and other research projects, and each notebook should be dedicated to a single activity or project. The use of stickers in each notebook to capture necessary information (e.g., unique identification number, project number, name of user, location, etc.) is recommended. A log of issuance should also be kept.

Quality of the scientific work. Although there is some overlap in the naming and assignment of tasks to the processes of the development and validation of a biological test method, most references agree that there are distinct stages, to which certain quality activities may be assigned. These stages will be discussed in this paper as development, optimization, establishment of the method, in-house validation and evaluation, collaborative trial, benchmarking, approval, transfer, and reevaluation.

Reference materials, controls, and statistical control. Once the project has been approved, development begins. During development, the selection of any reference materials or reference standards should be

made. Controls should also be selected and characterized. Initial statistical control should be established, and the process of optimization undertaken.

Optimization. Optimization may be defined as the process whereby many analytical characteristics of the method (e.g., intra-assay precision), critical specifications (e.g., for equipment and materials), critical control points (e.g., test conditions such as dilutions, pH ranges, temperature ranges), ranges of the critical control points (e.g., ± 0.10 pH units), and the process control or quality control needed at each critical control point is determined (e.g., check the temperature and if it is outside the allowed range, redo the test). Limits on controls are established and statistical control of the process confirmed. This is similar to the determination of *robustness*, the process of discovering the critical ranges within which various parameters may vary without affecting the validity of the method.⁶ Robustness is intended to be a measure of a method's capacity to remain unaffected by deliberate small variations in a method's parameters and thereby functions as a measure of a method's reliability during normal usage. Examples of components for optimization of a polymerase chain reaction method are template DNA concentrations, primer concentration, and thermocycling temperature ranges.

Sources of *measurement uncertainty*, "a parameter associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the *measurand*,"⁸ may also be determined at this stage. An example of a source of measurement uncertainty is the variation in isolation rate because of sample effects. An example of *measurand* is the concentration of antibody or microorganisms (i.e., concentration).

During this stage, an in-house assessment of ruggedness may also be obtained. *Ruggedness* is the capacity of an assay (method) to remain unaffected when small changes in environment or operating conditions are made.⁶ Some references equate ruggedness with robustness. In this case, robustness may be seen to be a measure of nonrandom variability (i.e., deliberate changes), and ruggedness, of random variability. Such in-house studies are meant to mimic different test environments and should include a study of between analyst variability. Once optimization is complete, the method must be documented as a procedure.

Documentation of the method. Documentation of the test method as a procedure is an important quality assurance activity. Requirements and guidelines for this are described in ISO/IEC 17025,¹⁶ from the Office International des Epizooties (OIE),¹⁸ and from the AOAC International.¹ The author recommends the following be included:

- Evidence of document and configuration control (e.g., a unique identification number and version number on each page, a record of approval by qualified staff, and a controlled copy or notification list for the document).
- A list of pertinent references.
- A description of scope (e.g., the commodity or group of animals).
- Limitations on applicability.
- Performance characteristics (e.g., diagnostic sensitivity).
- A description of the type of item, material, matrix or specimen to be tested, including species (e.g., equine serum).
- The minimum amount of sample required.
- The parameters or quantities to be determined (e.g., antibody titer, colony count, parts per billion) with the analytical range stated (e.g., 1–10 ppb).
- A description of the analyte or intended analyses (e.g., antibody) or both.
- A high level of descriptive detail.
- A clear and logical presentation.
- Critical specifications, tolerances, and any other critical details for equipment, instruments, apparatus, and software, including technical performance requirements (e.g., manufacturer, model number, accuracy, precision).
- Critical specifications for materials, reagents, chemicals, and other consumable materials (e.g., manufacturer, grade, formula weight).
- Critical specifications for reference standards and materials (e.g., reference strains).
- Special physical and environmental conditions needed, including biosecurity level.
- Conditions for acceptance of samples as fit for testing.
- Description of or reference to procedures for the identification, handling, transporting, preparation storage, and retention of samples.
- A full description of the test procedure.
- A description of or reference to reagent and media preparation and quality control, including criteria for acceptance or rejection of lots to be used in testing.
- A description of the necessary process control and quality control for the test, including checks to be made before starting, and action to be taken if limits or criteria are not met.
- A full description of the controls used and the limits on each.
- Criteria for acceptance or rejection of test results.
- The data to be recorded.
- The method of recording original observations and results (It is recommended a worksheet(s) be appended to each method.).
- The method of analysis and presentation of results, including a description of mathematical factors, calculations, and statistics, methods of data transformation (e.g., how optical density values are transformed to positive or negative), and the method of diagnostic interpretation (e.g., interpretation of titers as positive or negative).
- Procedures for measuring uncertainty, if applicable.
- Pertinent critical safety specifications and steps.

Validation

The in-house validation and evaluation. Once the test method has been documented, it may then be used to further evaluate itself. This step is commonly known as the (in-house) validation. Examples of ways of evaluating a method are listed below:

- Reproduction of data from a standard method, publication, laboratory, or researcher.
- Epidemiological studies or trials.
- Comparison with other methods.
- Comparison with reference materials or reference standards.
- Interlaboratory studies (analysis of tested samples from another laboratory).
- Proficiency testing.
- Training or exercise at a reference laboratory.
- Clinical studies or trials.

Of great importance to quality is what the in-house validation determines: diagnostic cutoffs and performance characteristics such as diagnostic and analytical sensitivity (accuracy and detectability), specificity (accuracy), and isolation rate (detectability, limit of detection) are defined. It is essential that the work done to determine such parameters is as accurate, precise, and thorough as costs, time, and availability of samples permit. It is advisable to calculate the confidence interval on these numbers (e.g., sensitivity = $99 \pm 0.5\%$). Some types of precision may also be determined at this step. It is also important to note that test results are being generated and therefore certain technical requirements of ISO/IEC 17025 apply (e.g., requirements for equipment and calibration). Records obtained from test runs should be the same as the records that are going to be generated for submitted samples (e.g., worksheets and control charts). It is also well known that the proper selection of the population of animals or samples with which to determine diagnostic performance characteristics is of great importance to quality. The selection of appropriate statistical methods and parameters to analyze the data is also critical in ensuring quality.

The collaborative trial. Many method developers

wisely try the method by testing at a beta (pilot study) site. Sometimes samples from other laboratories are used in the evaluation of the method and in the determination of performance characteristics. Such activities assist in evaluating the method for transferability and provide additional data concerning the method's performance characteristics. However, it is collaborative trials, also known as collaborative studies, that give the method recognition as being "fully validated."

In the collaborative trial, a number of different laboratories use the method to test a predetermined number of parallel or split samples. Results are compared, statistics obtained, and the data are used to determine expectations for performance at a user laboratory and to further define method ruggedness (e.g., between laboratory precision). The AOAC International and other organizations have very specific criteria for such trials.¹ The AOAC International's program is very well regarded nationally and internationally.

Benchmarking the method. In some situations, particularly those concerning trade issues, the method may have to be *benchmarked*, or compared with outside laboratories using proficiency testing or reference materials and standards or both, as agreed to by all parties. As previously mentioned, this may have already been done as part of the in-house validation and evaluation.

Approval

Client meetings and communications. As stated, clients should be given an opportunity to give their informed consent regarding the methods that will be developed and used for their testing needs. The client's needs must be properly identified and in a quality oriented organization, anticipated. The laboratory should specify in its policies and procedures all points at which clients must be consulted, notified, met with, and their approval obtained in the method's development, approval, and transfer process. The laboratory should also specify what information and data are to be made available to the client.

Approved status. Although approvals are obtained throughout the development and validation process as specified in the laboratory's policies and procedures, there should also be a final approval, involving the laboratory and, where appropriate, the client, after which the method is declared ready for transfer and use. In some organizations, this status is noted as "official." The laboratory should have policies and procedures that address the following:

- The steps through which the method development must have gone before being presented for approval.

- Criteria for validated and ready to transfer status (e.g., Is an in-house validation sufficient, and, if so, under what circumstances? Or, must there always be a collaborative trial? Are all methods to be benchmarked?).
- How approvers of methods are qualified and identified.
- The process by which the method, documentation, data, data summaries, and records are presented to reviewers and approvers, and the decisions that may be taken (e.g., ready for approval, need more detail, need more data, need more or different statistical analyses) by each.
- How the records and the documented method are reviewed for completeness, clarity, and sufficiency, and by whom, and who approves them for archiving.
- The requirements for which the approver denotes the "approved" or "official" status of the method.

Method transfer

Transfer into use. Transfer of a method from development and validation phases into testing and diagnostic use should be a formalized activity with policy and procedures that specify the process and criteria for successful completion of staff training and method transfer. Generally, the documented method, reagents, and reference materials are acquired, and analysts are trained in the new method. Hands-on training at the reference (i.e., developer or technically expert) laboratory is advisable if the method is technically complex. The method must be demonstrated as in statistical control in the user laboratory. This may be achieved by using the method to test reference materials or controls and by analyzing the results obtained using statistics and control charts. Proficiency with the method and the ability to get valid results should be demonstrated for each analyst by using blind proficiency testing.

Other validity issues

Trade and regulatory implications. Trade and regulatory requirements may add extra requirements to demonstrate that the method is valid in testing. Commonly this is done by benchmarking (see above), and by the accreditation of the laboratory that will use the method. The use of a fully validated or official method issued by a particular technical or governmental body may also be required. Accreditation in relationship to trade issues has been discussed previously.²²

Reevaluation of performance. ISO/IEC 17025 states, "The Laboratory shall inform the client when the method proposed by the client is considered to be inappropriate or out of date." Reassessment and re-

view for capability and improvement are important quality management activities. The laboratory should have policy and procedures that describe how methods will be re-evaluated for suitability. In veterinary testing, population dynamics must also be considered, and performance characteristics must be rechecked for validity at appropriate intervals or in response to events and issues. Epidemiological assessment and reassessment are important quality activities. Ultimately, the method will have to be assessed in parallel with newer methods and technology. Such reevaluations should be tied in to preplanned, scheduled communications and with the anticipated needs of the laboratory's clients. This then forms a closed loop or full cycle with **Selection of the Test Method.**

Guidance on method validation. The following organizations are some of the many reputable and experienced technical bodies that offer guidance and standards on test method development and validation. Examples of their publications are cited:

- ASTM International (formerly the American Society for Testing and Materials)²⁻⁵.
- The Analytical Environmental Immunochemical Consortium (AEIC)⁶.
- The AOAC International (formerly the Association of Official Analytical Chemists)¹.
- The Co-Operation on International Traceability in Analytical Chemistry (CITAC)^{7,8}.
- Eurachem¹⁰.
- International Cooperation on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH)¹².
- International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH)^{13,14}.
- The International Union of Pure and Applied Chemistry, IUPAC¹¹.
- OECD¹⁹.
- The National Committee for Clinical Laboratory Standards (NCCLS).
- OIE¹⁸.
- The Standards Council of Canada (SCC)²⁰.
- The United States Pharmacopeia (USP)²¹.

Accreditation for method development and validation. Some accreditation bodies offer accreditation for method development activities (e.g., SCC). Accreditation of a laboratory for competence to conduct method development and validation will assist the laboratory in ensuring the cost effective development and implementation of valid methods, as well as add credibility to method performance characteristics and test results.

Conclusions

Validation is no longer just an in-house issue for veterinary laboratories. No matter how carefully produced, a test result is meaningless if it cannot be reproduced, or if the data cannot support the validity of the performance characteristics of the test method. Many national and international organizations and standards address requirements and criteria for method development and validation. Trade and regulatory considerations promote the use of official methods, which must have documented and approved processes, including requirements, by which they become official. The inclusion of the requirement for validated methods in ISO/IEC 17025 makes this an important issue regarding laboratory accreditation and in the creation of laboratory systems and networks. The requirement for and interest in measurement uncertainty has also increased the importance of the quality assurance of method validation. Laboratories will therefore be required to some degree to demonstrate competence in the conduct of method development and evaluation, even if they only wish to be accredited for routine testing. Procedures for determining the validity and official status of a method will be more open to scrutiny, as will attendant records and data. It is therefore necessary for veterinary laboratories to view quality policy and procedures as an integral part of method development and approval for use, as well as to include these activities as an integral part of the production of test results and therefore within the scope of the laboratory's quality management system.

References

1. AOAC International (formerly the Association of Official Analytical Chemists): 2002, AOAC® *Official Methods*SM program manual (OMA program manual): a policies and procedures guide for the official methods of analysis program (OMA). AOAC International, Gaithersburg, MD.
2. ASTM International (formerly the American Society of Testing and Materials): 1989, Standard guide for conducting ruggedness tests (ASTM E 1169-89). ASTM International, West Conshohocken, PA.
3. ASTM International: 1990, Standard practice for use of the terms precision and bias in ASTM test methods (ASTM E 177-90). ASTM International, West Conshohocken, PA.
4. ASTM International: 1996, Standard terminology relating to quality and statistics (ASTM E 456-96). ASTM International, West Conshohocken, PA.
5. ASTM International: 1999, Standard practice for conducting an interlaboratory study to determine the precision of a test method (ASTM E 691-99). ASTM International, West Conshohocken, PA.
6. Charlton S, Giroux, R, Hondred D, et al.: 2000, PCR validation and performance characteristics—AEIC Biotech Consensus Paper. The Analytical Environmental Immunochemical Consortium (AEIC) Secretariat, Dow AgroSciences, Indianapolis, IN.
7. Co-Operation on International Traceability in Analytical Chemistry (CITAC): 1998, Eurachem/CITAC guide CG 2. quality as-

- insurance for research and development and nonroutine analysis. The CITAC Secretariat, IRMM, Geel, Belgium.
8. Co-Operation on International Traceability in Analytical Chemistry (CITAC): 2000, Eurachem/CITAC guide QUAM:2000.P1. Quantifying uncertainty in analytical measurement. The CITAC Secretariat, IRMM, Geel, Belgium.
 9. Day, P: 1999, The philosopher's tree, a selection of Michael Faraday's writings. Institute of Physics Publishing (IOPP), Bristol, UK.
 10. Eurachem: 1998, The fitness for purpose of analytical methods: a laboratory guide to method validation and related topics. Eurachem, Teddington, UK.
 11. Horwitz W: 1995, Protocol for the design, conduct and interpretation of method-performance studies. *Pure Appl Chem* 67: 331–343.
 12. International Cooperation on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH): 1996, Validation of analytical procedures: methodology (ICH-Q2B). ICH, Geneva, Switzerland, 27463–27467.
 13. International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH): 1999, Validation of analytical procedures: definition and terminology (VICH GL1). VICH Secretariat, Brussels, Belgium.
 14. International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH): 1999, Validation of analytical procedures: methodology (VICH GL2). VICH Secretariat, Brussels, Belgium.
 15. International Organization for Standardization (ISO): 1997, ISO international standard 10006: quality management—guidelines to quality in project management. ISO, Geneva, Switzerland.
 16. International Organization for Standardization (ISO): 1999, ISO/IEC international standard 17025. General requirements for the competence of testing and calibration laboratories. ISO, Geneva, Switzerland.
 17. Kanare, HM: 1985, Writing the laboratory notebook. American Chemical Society, Washington, DC.
 18. Office International des Epizooties (World Organisation for Animal Health): 2000, OIE manual of standards for diagnostic tests and vaccines, 4th ed. Office International des Epizooties, Paris, France.
 19. Organisation for Economic Co-operation and Development (OECD): 1997, OECD principles of good laboratory practice. The Organisation for Economic Cooperation and Development, OECD, Washington, D.C. OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, No. 1.
 20. Standards Council of Canada (SCC): 2001, CAN-P-1595: guidelines for the accreditation of laboratories engaged in test method development & evaluation and non-routine testing, version 1. Standards Council of Canada, Ottawa, Canada.
 21. USP (United States Pharmacopeia): 1999, Validation of compendial methods. USP 23, item 1225. United States Pharmacopoeial Convention, Inc., Rockville, MD.
 22. Wiegiers, AL: 2002, The “Age of Competence”: an update on the international laboratory accreditation scene for veterinary testing laboratories. *J Vet Diagn Investig* 14:89–96.